

OFFICIAL

AMENDMENTS TO THE SPECIFICATION

On page 1, lines 5-7, please delete: --

(Provisional Application Serial No.) _____ (Filing Date)

~~60/093,230~~ _____ ~~7/17/98~~ --

and substitute:

-- -- This application is a continuation of Application No. 09/234,606, filed January 21, 1999, which claims the benefit of U.S. Provisional Application No. 60/093,230, filed July 17, 1998. -- --

Applicants hereby submit a marked version of Specification Replacement Sheet to show changes made. Please enter replacement sheets. The Replacement Sheets do not contain new matter.

[REPLACEMENT SHEET]

Chelating Systems for Use in the Delivery of Compounds to Cells**CROSS-REFERENCE TO RELATED APPLICATIONS**

(Provisional Application Serial No.) (Filing Date)

5 ~~60/093,230~~ ~~7/17/98~~

This application is a continuation of Application No. 09/234,606, filed January 21, 1999, which claims the benefit of U.S. Provisional Application No. 60/093,230, filed July 17, 1998.

FEDERALLY SPONSORED RESEARCH

10 N/A

Field of the Invention

he invention relates to chelator-containing systems for use in biologic systems. More particularly, chelators and polychelators are utilized in the delivery of molecules, polymers,
15 nucleic acids and genes to cells.

Background

Polymers are used for drug delivery for a variety of therapeutic purposes. Polymers have also been used in research for the delivery of nucleic acids (polynucleotides and oligonucleotides)
20 to cells with an eventual goal of providing therapeutic processes. Such processes have been termed gene therapy or anti-sense therapy. One of the several methods of nucleic acid delivery to the cells is the use of DNA-polycation complexes. It has been shown that cationic proteins like histones and protamines or synthetic polymers like polylysine, polyarginine, polyornithine, DEAE dextran, polybrene, and polyethylenimine may be effective
25 intracellular delivery agents while small polycations like spermine are ineffective. The following are some important principles involving the mechanism by which polycations facilitate uptake of DNA:

Polycations provide attachment of DNA to the target cell surface. The polymer forms a
30 cross-bridge between the polyanionic nucleic acids and the polyanionic surfaces of the cells. As a result the main mechanism of DNA translocation to the intracellular space might be non-specific adsorptive endocytosis which may be more effective than liquid endocytosis or receptor-mediated endocytosis. Furthermore, polycations are a convenient linker for attaching specific